COCHRANE CORNER

Melatonin and agomelatine for preventing seasonal affective disorder: a Cochrane Review†

Barbara Nussbaumer-Streit, Amy Greenblatt, Angela Kaminski-Hartenthaler, Megan G. Van Noord, Catherine A. Forneris, Laura C. Morgan, Bradley N. Gaynes, Jörg Wipplinger, Linda J. Lux, Dietmar Winkler & Gerald Gartlehner

†This review is the abstract of a Cochrane Review previously published in the *Cochrane Database of Systematic Reviews*, 2019, Issue 6, Art. No.: CD011271, doi: 10.1002/14651858.CD011271.pub3 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the *Cochrane Database of Systematic Reviews* should be consulted for the most recent version of the review.

We thank the Cochrane Common Mental Disorders Group for their support in publishing these reviews.

See commentary in this issue.

Background

Seasonal affective disorder (SAD) is a seasonal pattern of recurrent major depressive episodes that most commonly starts in autumn or winter and remits in spring. The prevalence of SAD depends on latitude and ranges from 1.5% to 9%. The predictable seasonal aspect of SAD provides a promising opportunity for prevention in people who have a history of SAD. This is one of four reviews on the efficacy and safety of interventions to prevent SAD; we focus on agomelatine and melatonin as preventive interventions.

Objectives

To assess the efficacy and safety of agomelatine and melatonin (in comparison with each other, placebo, second-generation antidepressants, light therapy, psychological therapy or lifestyle interventions) in preventing SAD and improving person-centred outcomes among adults with a history of SAD.

Search methods

We searched Ovid MEDLINE (1950–), Embase (1974–), PsycINFO (1967–) and the Cochrane Central Register of Controlled Trials (CENTRAL) to 19 June 2018. An earlier search of these databases was conducted via the Cochrane Common Mental Disorders Controlled Trial Register (CCMD-CTR) (all years to 11 August 2015). Furthermore, we searched the Cumulative Index to Nursing and Allied Health Literature, Web of Science, the Cochrane Library, the Allied and Complementary Medicine Database and international trial registers (to 19 June 2018). We also conducted a grey literature search and handsearched the reference lists of included studies and pertinent review articles.

Selection criteria

To examine efficacy, we included randomised controlled trials (RCTs) on adults with a history of winter-type SAD who were free of symptoms at the beginning of the study. For adverse events, we intended also to include non-randomised studies. We planned to include studies that compared agomelatine versus melatonin, or agomelatine or melatonin versus placebo, any second-generation antidepressant, light therapy, psychological therapies or lifestyle changes. We also intended to compare melatonin or agomelatine in combination with any of the comparator interventions mentioned above versus the same comparator intervention as monotherapy.

Data collection and analysis

Two review authors screened abstracts and full-text publications, abstracted data and assessed risk of bias of included studies independently. We intended to pool data in a meta-analysis using a random-effects model, but included only one study.

Main results

We identified 3745 citations through electronic searches and reviews of reference lists after deduplication of search results. We excluded 3619 records during title and abstract review and assessed 126 full-text papers for inclusion in the review. Only one study, providing data of 225 participants, met our eligibility criteria and compared agomelatine (25 mg/day) with placebo. We rated it as having high risk of attrition bias because nearly half of the participants left the study before completion. We rated the certainty of the evidence as very low for all outcomes, because of high risk of bias, indirectness, and imprecision.

The main analysis based on data of 199 participants rendered an indeterminate result with wide confidence intervals (CIs) that may encompass both a relevant reduction as well as a relevant increase of SAD incidence by agomelatine (risk ratio (RR) 0.83, 95% CI 0.51 to 1.34; 199 participants; very low-certainty evidence). Also the severity of SAD may be similar in both groups at the end of the study with a mean SIGH-SAD (Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders) score of 8.3 (standard deviation (SD) 9.4) in the agomelatine group and 10.1 (SD 10.6) in the placebo group (mean difference (MD) –1.80, 95% CI –4.58 to 0.98; 199 participants; very low-certainty evidence). The incidence of adverse events and serious adverse events may be similar in both groups. In the agomelatine group, 64 out of 112 participants experienced at least one adverse event, while 61 out of 113 did in the placebo group (RR 1.06, 95% CI 0.84 to 1.34; 225 participants; very low-certainty evidence). Three out of 112 patients experienced serious adverse events in the agomelatine group, compared to 4 out of 113 in the placebo group (RR 0.76, 95% CI 0.17 to 3.30; 225 participants; very low-certainty evidence).

No data on quality of life or interpersonal functioning were reported. We did not identify any studies on melatonin.

Authors' conclusions

Given the uncertain evidence on agomelatine and the absence of studies on melatonin, no conclusion about efficacy and safety of agomelatine and melatonin for prevention of SAD can currently be drawn. The decision for or against initiating preventive treatment of SAD and the treatment selected should consider patient preferences and reflect on the evidence base of all available treatment options.

https://doi.org/10.1192/bja.2020.26 Published online by Cambridge University Press